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## Relationship of Macronutrients and Physical Activity to Chronic Disease

### OVERVIEW

Over the last 40 years, a growing body of evidence has accumulated regarding the relationships among consumption of dietary fat, carbohydrate, protein, and energy and risk of chronic disease. The fact that diets are usually composed of a variety of foods that include varying amounts of carbohydrate, protein, and various fats imposes some limits on the type of research that can be conducted to ascertain causal relationships. The available data regarding the relationships among major chronic diseases that have been linked with consumption of dietary energy and macronutrients (fats, carbohydrates, fiber, and protein), as well as physical inactivity, are discussed below and are reviewed in greater detail in the specific nutrient chapters (Chapters 5 through 11) and the chapter on physical activity (Chapter 12).

### CANCER

Diet has long been suspected as a cancer-causing agent. Early studies in animals showed that diet could influence carcinogenesis (Tannenbaum, 1942; Tannenbaum and Silverstone, 1957). Cross-cultural studies that compare incidence rates of specific cancers across populations have found great differences in cancer incidence, and dietary factors, at least in part, have been implicated as causes of these differences (Armstrong and Doll, 1975; Gray et al., 1979; Rose et al., 1986). In addition, observational studies have found strong correlations among dietary components and incidence and mortality rates of cancer (Armstrong and Doll, 1975).

Associations among dietary fat, carbohydrates, and protein and cancer have been hypothesized. Many of these associations, however, have not been supported by clinical and interventional studies in humans.

Increased intakes of energy, total fat, *n*-6 polyunsaturated fatty acids, cholesterol, sugars, protein, and some amino acids have been thought to increase the risk of various cancers, whereas intakes of *n*-3 fatty acids, dietary fiber, and physical activity are thought to be protective. The major findings and potential mechanisms for these relationships are discussed below.

### *Energy*

Animal studies suggest that restriction of energy intake may inhibit cell proliferation (Zhu et al., 1999) and tumor growth (Wang et al., 2000). A risk of mortality from cancer has been associated with increased energy intakes during childhood (Frankel et al., 1998; Must and Lipman, 1999). Excess energy intake is a contributing factor to obesity, which is thought to increase the risk of certain cancers (Carroll, 1998). To support this concept, a number of studies have observed a positive association between energy intake during adulthood and risk of cancer (Andersson et al., 1996; Lissner et al., 1992; Lyon et al., 1987), whereas other studies did not find an association (Stemmermann et al., 1985).

### *Dietary Fat*

High intakes of dietary fat have been implicated in the development of certain cancers. Early cross-cultural and case-control studies reported strong associations between total fat intake and breast cancer (Howe et al., 1991; Miller et al., 1978; van't Veer et al., 1990), yet a number of epidemiological studies, most in the last 15 years, have found little or no association (Hunter et al., 1996; Jones et al., 1987; Kushi et al., 1992; van den Brandt et al., 1993; Velie et al., 2000; Willett et al., 1987, 1992). Evidence from epidemiological studies on the relationship between fat intake and colon cancer has been mixed as well (De Stefani et al., 1997b; Giovannucci et al., 1994; Willett et al., 1990). Howe and colleagues (1997) reported no association between fat intake and risk of colorectal cancer from the combined analysis of 13 case-control studies. Epidemiological studies tend to suggest that dietary fat intake is not associated with prostate cancer (Ramon et al., 2000; Veierød et al., 1997b). Giovannucci and coworkers (1993), however, reported a positive association between total fat consumption, primarily animal fat, and risk of advanced prostate cancer. Findings on the association between fat intake and lung cancer have been mixed (De Stefani et al., 1997a; Goodman et al., 1988; Veierød et al., 1997a; Wu et al.,

1994). Numerous mechanisms for the carcinogenic effect of dietary fat have been proposed, including eicosanoid metabolism, cellular proliferation, and alteration of gene expression (Birt et al., 1999).

Experimental evidence suggests several mechanisms in which *n*-3 fatty acids may protect against cancer. *n*-3 Fatty acids, particularly docosahexaenoic acid and eicosapentaenoic acid, have been shown to suppress neoplastic transformation (Takahashi et al., 1992), inhibit cell growth and proliferation (Anti et al., 1992; Calviello et al., 1998; Grammatikos et al., 1994), induce apoptosis (Calviello et al., 1998; Lai et al., 1996), and inhibit angiogenesis (Rose and Connolly, 2000), which may occur by suppressing *n*-6 fatty acid eicosanoid production. Epidemiological studies have shown an inverse relationship between fish consumption and the risk of breast and colorectal cancer (Caygill and Hill, 1995; Caygill et al., 1996; Kaizer et al., 1989; Sasaki et al., 1993; Willett et al., 1990).

Monounsaturated fatty acids have been reported as being protective against breast, colon, and possibly prostate cancer (Bartsch et al., 1999). However, there is also some epidemiological evidence for a positive association between these fatty acids and breast cancer risk in women with no history of benign breast disease (Velie et al., 2000) and prostate cancer in men (Schuurman et al., 1999). There may be protective effects associated with olive oil (Rose, 1997; Trichopoulou et al., 1995; Willett, 1997); however, these benefits may reflect constituents other than monounsaturated fatty acids.

### *Dietary Carbohydrate*

While the data on sugar intake and cancer are limited and insufficient, several case-control studies have shown an increased risk of colorectal cancer among individuals with high intakes of sugar-rich foods (Benito et al., 1990; Macquart-Moulin et al., 1986, 1987; Tuyns et al., 1988). Additionally, high vegetable and fruit consumption and avoidance of foods containing highly refined sugars were shown to be negatively correlated to the risk of colon cancer (Giovannucci and Willett, 1994).

### *Dietary Fiber*

There is some evidence based on observational and case-control studies that fiber-rich diets are protective against colorectal cancer (Lanza, 1990; Trock et al., 1990). There is also some epidemiological evidence of a protective effect of cereals and cereal fiber against colon carcinogenesis (Hill, 1997). Despite these and other positive findings, a number of important studies (Fuchs et al., 1999; Giovannucci and Willett, 1994) and three recent clinical intervention trials (Alberts et al., 2000; Bonithon-Kopp et al., 2000;

Schatzkin et al., 2000) do not support a protective effect of dietary fiber against colon cancer, and the issue remains to be resolved.

High-fiber diets may also be protective against the development of colonic adenomas (Giovannucci et al., 1992; Hoff et al., 1986; Little et al., 1993; Macquart-Moulin et al., 1987; Neugut et al., 1993). However, not all studies have found a significant association between the dietary intake of total, cereal, or vegetable fiber and colorectal adenomas, although a slight reduction in risk was observed with increasing intake of fruit fiber (Platz et al., 1997).

There are numerous hypotheses as to how fiber might protect against the development of colon cancer. These include the dilution of carcinogens, procarcinogens, and tumor promoters in a bulky stool; a more rapid rate of transit through the colon with high-fiber diets; a reduction in the ratio of secondary bile acids to primary bile acids by acidifying colonic contents; the production of butyrate from the fermentation of dietary fiber by the colonic microflora; and the reduction of ammonia, which is known to be toxic to cells (Harris and Ferguson, 1993; Jacobs, 1986; Klurfeld, 1992; Van Munster and Nagengast, 1993; Visek, 1978).

Fiber has been shown to lower serum estrogen concentrations (Rose et al., 1991), and therefore may have a protective effect against hormone-related cancers. Recent studies have shown a decreased risk of endometrial cancer (Barbone et al., 1993; Goodman et al., 1997), ovarian cancer (Risch et al., 1994; Tzonou et al., 1993), and prostate cancer (Andersson et al., 1996) with high fiber intakes. More research is needed before conclusions can be drawn on these relationships.

Although fiber has the ability to decrease blood estrogen concentrations by a variety of different mechanisms (Rose et al., 1991), it is not yet known whether this action is sufficient to decrease the risk of breast cancer. Half of the epidemiological studies attempting to link low dietary fiber intake to breast cancer have failed to show this relationship (Gerber, 1998). The data on cereal intake and breast cancer risk are considerably stronger than overall fiber intake (Rohan et al., 1993), suggesting that certain cereal foods are protective or that only certain types and stages of breast cancer respond to these interventions.

### *Physical Activity*

Regular exercise, as recommended in this report, has been shown to be negatively correlated with the risk of colon cancer (Colbert et al., 2001; White et al., 1996). This is, in part, due to the reduction in obesity, which is positively related to cancer (Carroll, 1998). In men and women who are physically active, the risk of colon cancer is reduced by 30 to 40 percent compared with those who are sedentary. A plausible mechanism for the

effect of physical activity on colon cancer is the shortening of intestinal transit time, thus reducing contact time between intestinal mucosa and carcinogens and mutagens in the diet that are carried in the fecal stream (Batty and Thune, 2000).

Examination of more than 30 epidemiological studies concluded that regular physical activity decreased the risk of breast cancer by 20 to 40 percent (IARC, 2002). However, relatively few studies found a consistent association between physical activity and decreased incidence of endometrial cancer. For prostate cancer, results of about 20 studies were less consistent, with only moderately strong relationships. As endogenous sex steroids have been implicated in the development of breast, endometrial, and prostate cancers, a plausible explanation for the inverse relationship among physical activity and reproductive organ cancers may involve the effect of exercise on the binding and turnover of sex steroids and glucoregulatory hormones, as well as the overall effect of exercise on body fat (IARC, 2002; Vainio and Bianchini, 2001).

With regard to the possible effect of exercise on other forms of cancer, such as pancreatic cancer (Michaud et al., 2001), exercise may also play a beneficial role by compensating for effects of excess energy intake; by modifying the effects of carcinogens, cocarcinogens, and cancer promoters; or by decreasing body fat and lessening the accumulation of cancer-causing substances in body tissues (Shephard, 1990, 1996). Regular activity may also bolster the immune system (Bruunsgaard et al., 1999; Mazzeo et al., 1998).

## HEART DISEASE

The known risk factors for coronary heart disease (CHD) include high serum low density lipoprotein (LDL) cholesterol concentration, low serum high density lipoprotein (HDL) cholesterol concentration, a family history of CHD, hypertension, diabetes mellitus, cigarette smoking, advancing age, and obesity (Castelli, 1996; Hennekens, 1998; Parmley, 1997). There is a positive linear relationship between serum total cholesterol and LDL cholesterol concentrations and risk of CHD or mortality from CHD (Jousilahti et al., 1998; Neaton and Wentworth, 1992; Sorkin et al., 1992; Stamler et al., 1986). A low concentration of HDL cholesterol is positively correlated with risk of CHD, independent of other risk factors (Austin et al., 2000).

High concentrations of serum triacylglycerol may also contribute to CHD (Austin, 1989), but the evidence is less clear. Most studies show a positive relationship between serum triacylglycerol and CHD (Bainton et al., 1992; Carlson and Böttiger, 1972; Gordon et al., 1977; Hulley et al., 1980; Stampfer et al., 1996); however, Gordon and coworkers (1977) found

that the statistical significance of this relationship disappears after controlling for total cholesterol, LDL cholesterol, or HDL cholesterol.

The role of diet in the promotion or prevention of heart disease is the subject of considerable research. New studies investigating dietary energy sources and physical activity for their potential to alter some of the risk factors for heart disease are underway (i.e., plasma cholesterol, hypertension, obesity, and diabetes).

### *Dietary Fat*

Increasing the intake of saturated fat can increase serum total cholesterol and LDL cholesterol concentrations (Clarke et al., 1997; Hegsted et al., 1993; Kasim et al., 1993; Krauss and Dreon, 1995; Mensink and Katan, 1992). Furthermore, a meta-analysis of 37 intervention studies showed that a reduction in plasma total cholesterol and LDL cholesterol concentrations was correlated with reductions in percentages of total dietary fat that also included a decrease in saturated fats (Yu-Poth et al., 1999). The correlation between total fat and serum cholesterol concentration is due, in part, to the strong positive association between total fat and saturated fat intake and the weak association between total fat and polyunsaturated fat intake (Masironi, 1970; Stamler, 1979). Furthermore, the impact of saturated fats in increasing LDL cholesterol concentration is twofold greater than the impact of polyunsaturated fats in reducing LDL cholesterol (Hegsted et al., 1993; Mensink and Katan, 1992). This effect, however, is not seen with all saturated fatty acids. While lauric, myristic, and palmitic acids increase cholesterol concentration (Mensink et al., 1994), stearic acid has been shown to have a neutral effect (Bonanome and Grundy, 1988; Denke, 1994; Yu et al., 1995).

Similar to saturated fat, increasing intakes of *trans* fatty acids and cholesterol increase serum total cholesterol and LDL cholesterol concentrations (Ascherio et al., 1999; Clarke et al., 1997; Hegsted, 1986; Howell et al., 1997). Epidemiological studies have generally demonstrated a positive association between *trans* fatty acid intake and increased risk of heart disease (Ascherio et al., 1994, 1996b; Hu et al., 1997; Pietinen et al., 1997; Willett et al., 1993); however, the risk with cholesterol intake has been mixed (Ascherio et al., 1996b; Hu et al., 1997, 1999b; Kushi et al., 1985; Mann et al., 1997; Pietinen et al., 1997). There is wide interindividual variation in serum cholesterol response to dietary cholesterol (Hopkins, 1992), which may be due to genetic factors.

Monounsaturated and polyunsaturated fatty acids decrease serum total cholesterol and LDL cholesterol concentrations (Gardner and Kraemer, 1995). The epidemiological data indicate that monounsaturated fats are either not associated or are positively associated with risk of CHD (Hu et

al., 1997; Kromhout and de Lezenne Coulander, 1984; Pietinen et al., 1997). High intakes of *n*-6 polyunsaturated fats have been associated with the reduced total cholesterol and LDL cholesterol concentrations that are associated with low risk of CHD (Arntzenius et al., 1985; Becker et al., 1983; Sonnenberg et al., 1996). In general, epidemiological studies have demonstrated an inverse association between *n*-6 polyunsaturated fatty acid intake and risk of CHD (Arntzenius et al., 1985; Gartside and Glueck, 1993).

*n*-3 Polyunsaturated fatty acids (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) have been shown to reduce the risk of CHD and stroke by a multitude of mechanisms: by preventing arrhythmias (Billman et al., 1999; Kang and Leaf, 1996; McLennan, 1993), reducing atherosclerosis (von Schacky et al., 1999), decreasing platelet aggregation (Harker et al., 1993), lowering plasma triacylglycerol concentrations (Harris, 1989), decreasing proinflammatory eicosanoids (James et al., 2000), modulating endothelial function (De Caterina et al., 2000), and decreasing blood pressure in hypertensive individuals (Morris et al., 1993). Many epidemiological studies have used fish or fish oil intake as a surrogate for *n*-3 fatty acid intake because of the high content of EPA and DHA found in fish. A number of these studies have concluded that fish consumption reduced the risk of CHD mortality (Daviglus et al., 1997; Dolecek, 1992; Kromhout et al., 1985, 1995), while others found no association (Albert et al., 1998; Ascherio et al., 1995).

### *Dietary Carbohydrate*

High carbohydrate (low fat) intakes tend to increase plasma triacylglycerol and decrease plasma HDL cholesterol concentrations (Borkman et al., 1991; Brussaard et al., 1982; Marckmann et al., 2000; West et al., 1990; Yost et al., 1998). This effect has been observed especially for increased sugar intake (Mann et al., 1973; Rath et al., 1974; Reiser et al., 1979; Yudkin et al., 1986). Fructose is a better substrate for *de novo* lipogenesis than glucose or starches (Cohen and Schall, 1988; Reiser and Hallfrisch, 1987), and Parks and Hellerstein (2000) concluded that hypertriacylglycerolemia is more extreme if the carbohydrate content of the diet consists primarily of monosaccharides, particularly fructose.

### *Dietary Fiber*

Evidence supports a protective effect of dietary fiber for CHD, particularly viscous fibers that occur naturally in foods, which reduce total cholesterol and LDL cholesterol concentrations (see Chapter 7). Reduced rates of CHD were observed in individuals consuming high fiber diets (Jacobs et al., 1998; Kushi et al., 1985; Pietinen et al., 1996). These studies used fiber-

containing foods; fiber supplements may not have the same effects. The type of fiber is important; oat bran (viscous fiber) significantly reduces total cholesterol, but wheat bran (primarily nonviscous fiber) may not (Behall, 1990). Viscous fibers are thought to lower serum cholesterol concentrations by interfering with absorption and recirculation of bile acids and cholesterol in the intestine and thus decreasing the concentration of circulating cholesterol. These fibers may also work by delaying absorption of fat and carbohydrate, which could result in increased insulin sensitivity (Hallfrisch et al., 1995) and lower triacylglycerol concentrations (Rivellese et al., 1980). Dietary fiber intake has also been shown to be negatively associated with hypertension in men (Ascherio et al., 1992), but not women (Ascherio et al., 1996a). Fiber intake was shown to have an inverse relationship with systolic and diastolic pressures (Ashcerio et al., 1996a).

### *Dietary Protein*

An inverse relationship between protein intake and risk of CHD has been observed (Hu et al., 1999a). High protein intake has been shown to lower blood pressure (Obarzanek et al., 1996), and substitution of carbohydrate with protein resulted in lower LDL cholesterol and triacylglycerol concentrations (Wolfe and Piché, 1999). These results may, however, be confounded by the fact that dietary animal protein and dietary fat tend to be highly correlated. Independent effects of protein on CHD mortality have not been shown (Gordon et al., 1981; Keys et al., 1986). Soy-based protein may reduce serum cholesterol concentrations, but the evidence has been mixed (Anderson et al., 1995; Bakhit et al., 1994; Meinertz et al., 1989; van Raaij et al., 1982).

### *Physical Activity*

Exercise improves and maintains vessel function. An inverse relationship between exercise and CHD mortality has been observed in numerous studies (Arraiz et al., 1992; Kannel et al., 1986; Lindsted et al., 1991; Paffenbarger et al., 1984). Regular exercise increases serum HDL cholesterol, decreases serum triacylglycerol, decreases blood pressure, enhances fibrinolysis, lessens platelet adherence, enhances glucose effectiveness and insulin sensitivity, and decreases risk of cardiac arrhythmias (Araújo-Vilar et al., 1997; Arroll and Beaglehole, 1992; El-Sayed, 1996; Hinkle et al., 1988; Huttunen et al., 1979).

The mechanisms by which exercise serves to mitigate progression of cardiovascular disease (CVD) and coronary artery disease (CAD) are numerous. For instance, patients with CAD who participated in exercise training showed improved endothelium-dependent vasodilatation in epi-

cardial coronary vessels and in resistance vessels (Hambrecht et al., 2000). Thus, exercise serves to maintain conduit function in vessels impacted by CAD. An inverse dose–response relationship between physical activity and physical fitness and CVD mortality has been documented (Arraiz et al., 1992; Blair et al., 1993; Kannel and Sorlie, 1979; Kannel et al., 1986; Lindsted et al., 1991; Paffenbarger et al., 1984).

Activity may also influence CVD indirectly via an influence on lipoprotein metabolism. Vigorous physical activity increases plasma HDL cholesterol, HDL<sub>2</sub>, and apolipoprotein A-I and decreases plasma triacylglycerol, very low density lipoprotein, and atherogenic small, dense LDL concentrations (Williams et al., 1986, 1990, 1992; Wood et al., 1988). Gradient gel electrophoresis shows that the protective HDL<sub>2b</sub> subclass is increased while the HDL<sub>3b</sub> subclass is decreased through exercise (Williams et al., 1992). The distribution of LDL is shifted toward larger and more buoyant particles of lower density that result in a decrease in the prevalence of the small, dense LDL phenotype among vigorously active men (Williams et al., 1990). Cross-sectional comparisons of high mileage and low mileage runners suggest that the benefits of vigorous exercise on the lipoprotein profile increase linearly with exercise dose through at least 40 mi (64 km)/wk for both HDL cholesterol and triacylglycerol (Williams, 1997). Physical activity prevents the rise in plasma triacylglycerols in individuals who consume high carbohydrate diets (Koutsari et al., 2001).

Many of the exercise-induced changes in lipoproteins may arise from the effects of lipolytic enzymes on lipoprotein size and composition, namely increases in lipoprotein lipase activity and decreases in hepatic lipase activity (Williams et al., 1986). Runners have significantly higher lipoprotein lipase activity in both muscle and adipose tissue (Nikkilä et al., 1978). Weight loss is known to both increase lipoprotein lipase and reduce hepatic lipase (Marniemi et al., 1990; Purnell et al., 2000). This may explain, in part, why increases in HDL cholesterol and HDL<sub>2</sub> mass in sedentary men who begin exercising vigorously are strongly associated with loss of body fat (Williams et al., 1983). Lipoprotein lipase activity may also explain why HDL cholesterol concentrations in sedentary men predict their success at running (Williams et al., 1994). Specifically, the enzyme's activity is positively correlated with HDL cholesterol concentrations and is higher in slow-twitch red muscle fibers. Thus, high HDL concentrations may be a marker for muscle fiber composition that facilitates endurance exercise.

## DENTAL CARIES

Sugars play an important role in dental caries development (Walker and Cleaton-Jones, 1992). Sugars provide a favorable environment for bac-

teria in the mouth, and the presence of these sugars increases the rate and volume of plaque formation (Depaola et al., 1999). However, because development of caries involves other factors such as fluoride intake, oral hygiene, food composition, and frequency of meals and snacks, sugar intake alone is not the only cause of caries.

## TYPE 2 DIABETES MELLITUS

Type 2 diabetes mellitus is characterized by a genetic predisposition to the disorder, decreased tissue sensitivity to insulin (insulin resistance), and impaired function of pancreatic  $\beta$ -cells, which control the timely release of insulin (Anderson, 1999). Obesity, physical inactivity, and advancing age are primary risk factors for insulin resistance and development of type 2 diabetes (Barrett-Connor, 1989; Colditz et al., 1990; Helmrach et al., 1991; Manson et al., 1991). Dietary factors have also been suggested as playing a major role in the development of insulin resistance and type 2 diabetes.

### *Dietary Fat*

Intervention studies that have evaluated the effect of the level of fat intake on biochemical risk factors for diabetes have been mixed (Abbott et al., 1989; Borkman et al., 1991; Coulston et al., 1983; Fukagawa et al., 1990; Howard et al., 1991; Jeppesen et al., 1997; Leclerc et al., 1993; Straznicky et al., 1999; Swinburn et al., 1991; Thomsen et al., 1999; Yost et al., 1998). Some epidemiological studies have shown a correlation between higher fat intakes and insulin resistance (Marshall et al., 1991; Mayer-Davis et al., 1997; Parker et al., 1993). It is not clear, however, whether the correlation is due to fat in the diet or to obesity. Obesity, particularly abdominal obesity, is a risk factor for type 2 diabetes (Vessby, 2000). Decreased physical activity is also a significant predictor of higher post-prandial insulin concentrations and may confound some studies (Feskens et al., 1994; Parker et al., 1993).

Findings from intervention studies tend to suggest a lack of adverse effect of saturated fat on risk indicators of diabetes in healthy individuals (Fasching et al., 1996; Roche et al., 1998; Thomsen et al., 1999). However, it was recently reported that the consumption of saturated fatty acids can significantly impair insulin sensitivity (Vessby et al., 2001).

Because of the favorable effects of *n*-3 fatty acids (eicosapentaenoic acid and docosahexaenoic acid) on risk indicators of coronary heart disease, they are often used in patients with lipid disorders. There has been concern about the use of these fatty acids for lipid disorders because many of these patients also have type 2 diabetes. A number of studies have sug-

gested that *n*-3 polyunsaturated fatty acid intake may have adverse effects in individuals with type 2 diabetes (Glauber et al., 1988; Kasim et al., 1988), requiring increased doses of hypoglycemic agents (Friday et al., 1989; Stacpoole et al., 1989; Zambon et al., 1992).

### *Dietary Carbohydrate*

There is little evidence that total dietary carbohydrate intake is associated with type 2 diabetes (Colditz et al., 1992; Lundgren et al., 1989). There may be an increased risk, however, when the glycemic index of a meal is considered instead of total carbohydrates (Salmerón et al., 1997a, 1997b). Some studies have found that reducing the glycemic index of a meal can result in short-term improved glucose tolerance and insulin sensitivity in healthy individuals (Frost et al., 1998; Jenkins et al., 1988; Liljeberg et al., 1999; Wolever et al., 1988). Additional long-term studies are needed to elucidate the true relationship between glycemic index and the development of type 2 diabetes and to determine its effect on glucose tolerance and insulin.

### *Dietary Fiber*

Certain dietary fibers may attenuate the insulin response and thus be protective against type 2 diabetes. There is good epidemiological evidence for the protective effect of fiber against type 2 diabetes (Colditz et al., 1992; Meyer et al., 2000; Salmerón et al., 1997a, 1997b). Viscous soluble fibers, such as pectin and guar gum, have been found to produce a significant reduction in glycemic response in the majority of studies reviewed by Wolever and Jenkins (1993). It is believed that viscous soluble fibers reduce the glycemic response of food by delaying gastric emptying and therefore delaying the absorption of glucose (Jenkins et al., 1978; Wood et al., 1994).

### *Physical Activity*

Increased levels of physical activity have been found to improve insulin sensitivity in individuals with type 2 diabetes (Horton, 1986; Mayer-Davis et al., 1998; Schneider et al., 1984). Physical inactivity was found to be associated with increased incidence of type 2 diabetes in cross-sectional (King et al., 1984; Taylor et al., 1983), cohort (Helmrich et al., 1991; Manson et al., 1991, 1992), and longitudinal training studies (Tuomilehto et al., 2001). Short- and long-term effects of physical activity on glucose tolerance, insulin action, and muscle glucose uptake show that contracting muscle has an "insulin-like" effect on promoting glucose uptake and metabolism (Bergman et al., 1999; Horton, 1991; Richter et al., 1981). This synergistic

effect of contractions on insulin action is thought to increase insulin action and decrease circulating glucose and insulin concentrations. Further, by increasing muscle mass, decreasing total and abdominal obesity (Björntorp et al., 1979; Després et al., 1988), and diverting dietary carbohydrate to muscle for oxidation and glycogen repletion (Brooks et al., 2000), physical activity reduces the potential for energy intakes exceeding expenditures, leading to fat accumulation. Physical activity can reduce the risk of type 2 diabetes (Diabetes Prevention Program Research Group, 2002; Tuomilehto et al., 2001), and can also reduce total and abdominal obesity, both of which are risk factors for type 2 diabetes (Vessby, 2000).

## OBESITY

Obesity results from an imbalance between energy intake and energy expenditure. The health risks associated with obesity include increased mortality, hypertension, cardiovascular disease, diabetes mellitus, gallbladder disease, some cancers, and changes in endocrine function and metabolism (NHLBI/NIDDK, 1998). The risk factors for becoming obese are not entirely understood but are thought to include genetics, food intake, physical inactivity, and some rare metabolic disorders (NHLBI/NIDDK, 1998).

### *Dietary Fat*

The available data on whether diets high in total fat increase the risk for obesity are conflicting and are complicated by underreporting of food intake, notably fat intake (Bray and Popkin, 1998; Lissner and Heitmann, 1995; Lissner et al., 2000; Willett, 1998). Intervention studies have shown that high-fat diets, as compared with low-fat diets with equivalent energy intake, are not intrinsically fattening (Davy et al., 2001), whereas cross-cultural, animal, and some human studies have provided support for the theory that diets with a high percentage of fat increase the risk of obesity (Astrup et al., 1997; Lissner and Heitmann, 1995; West and York, 1998). Other studies have shown that as the proportion of fat in the diet increases, so does energy intake (Kendall et al., 1991; Lissner et al., 1987; Stubbs et al., 1995). Because energy density was not kept separate from fat content in these studies, recent investigators have questioned the conclusions of these studies and have found differing results. Further studies have shown that fat content does not affect energy intake (Saltzman et al., 1997; Stubbs et al., 1996; van Stratum et al., 1978), and that energy density has an effect on energy intake independent of the fat content of the diet (Bell et al., 1998).

### *Dietary Carbohydrate*

A negative correlation between total sugars intake and body mass index has been reported in adults (Dreon et al., 1988; Dunnigan et al., 1970; Fehily et al., 1984; Gibson, 1993, 1996b; Miller et al., 1990). Increased added sugars intakes have been shown to result in increased energy intakes of children and adults (see Chapter 6) (Bowman, 1999; Gibson, 1996a, 1997; Lewis et al., 1992). In spite of this, a negative correlation between added sugars intake and body mass index has been observed in children (Bolton-Smith and Woodward, 1994; Gibson, 1996a; Lewis et al., 1992). Published reports disagree about whether a direct link exists between the trend toward higher intakes of sugars and increased rates of obesity. Any association between added sugars intake and body mass index is, in all likelihood, masked by the pervasive and serious problem of underreporting, which is more prevalent and severe among the obese population. In addition, foods and beverages high in added sugars are more likely to be underreported compared to other foods that may be perceived as “healthy” (Johnson, 2000).

### *Dietary Fiber*

Consumption of soluble fibers, which are low in energy, delays gastric emptying (Roberfroid, 1993), which in turn can cause an extended feeling of fullness and therefore satiety (Bergmann et al., 1992). A number of intervention studies suggest that diets high in fiber may assist in weight loss (Birketvedt et al., 2000; Eliasson et al., 1992; Rigaud et al., 1990; Rössner et al., 1987; Rytting et al., 1989), although other studies have not found this effect (Astrup et al., 1990; Baron et al., 1986). Thus, the evidence to support a role of fiber in the prevention of obesity is unclear at this time.

### *Physical Activity*

Energy expenditure by physical activity (see Chapters 5 and 12) varies considerably between individuals, affecting the energy balance and the body composition by which energy balance and weight maintenance are achieved (Ballor and Keese, 1991; Williamson et al., 1993). Indeed, physical inactivity is a major risk factor for development of obesity in children and adults (Astrup, 1999; Goran, 2001). In one study, increasing the level of physical activity in obese individuals appeared to have no effect on food intake, whereas in normal-weight individuals an increase in activity was coupled with an increase in food intake (Pi-Sunyer and Woo, 1985).

## SKELETAL HEALTH

Physical activity has a beneficial effect on bone health in individuals of all ages (Anderson, 2000; French et al., 2000; Hurley and Roth, 2000; Khan et al., 2000; Layne and Nelson, 1999; Madsen et al., 1998). Physical activity increases bone mass in children and adolescents and maintains bone mass in adults (French et al., 2000; Khan et al., 2000). In elderly individuals, bone mineral density has been found to be higher in those who exercise than in those who do not (Hurley and Roth, 2000). The same is true for young athletes compared to nonathletes (Madsen et al., 1998). Physical activity results in muscle strength, coordination, and flexibility that may benefit elderly individuals by preventing falls and fractures.

## SUMMARY

Many causal relationships among over- or underconsumption of macronutrients, physical inactivity, and chronic disease have been proposed. When the diet is modified for one energy-yielding nutrient, it invariably changes the intake of other nutrients, which makes it extremely difficult to have adequate substantiating evidence for providing clear and specific nutritional guidance. Acceptable Macronutrient Distribution Ranges can be estimated, however, by considering risk of chronic disease, as well as in the context of consuming adequate amounts of essential macronutrients and micronutrients. This information is provided in detail in Chapter 11.

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